

**IN THE CLAIMS**

**PLEASE AMEND THE CLAIMS AS FOLLOWS:**

1-30. (CANCELLED)

31. (PREVIOUSLY PRESENTED) A method of detecting blood flow abnormality or variation in a vessel or tissue comprising:

administering a contrast enhancing amount of a paramagnetic metal containing magnetic resonance magnetic resonance contrast agent into a vessel of a body;

imaging at least a portion of the body through which the MR contrast agent passes, with a MR imaging technique, thereby collecting temporally spaced sets of 3-D and 2-D data, each data set collected successively through an acquisition time;

forming a time sequence of image data including early image data and later image data;

comparing 3-D and 2-D data from the temporally spaced sets set of data by evaluating 2-D and 3-D temporally acquired images by comparing ones of said early image data within said acquisition time with ones of said later image data within said acquisition time and their intensity to assess blood flow or angiographic abnormality or variation.

32. (CANCELLED)

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34. (CANCELLED)

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36. (CANCELLED)

37. (PREVIOUSLY PRESENTED) A method of detecting blood flow abnormality or variation, in a human body, said method comprising the steps of:

administering into vasculature of said human body a contrast enhancing amount of a paramagnetic metal containing magnetic resonance contrast agent;

subjecting said human body to a magnetic resonance image procedure capable of generating from magnetic resonance signals from said human body successive images of temporally spaced images taken over an acquisition time period of at least part of said human body into which said contrast agent passes, said procedure being a magnetic resonance imaging procedure;

detecting temporal variations in said signals or images; and

from said temporal variations identifying regions of abnormal or modified blood flow in said human body and providing a quantitative indication of blood flow abnormality or variation.

38. (PREVIOUSLY PRESENTED) A method of detecting and quantitatively evaluating the severity of blood flow abnormality in a human body, said method comprising the steps of:

administering into vasculature of said human body a contrast enhancing amount of a paramagnetic metal containing magnetic resonance contrast agent;

subjecting said human body to a magnetic resonance image procedure capable of generating from magnetic resonance signals from said human body successive images of temporally spaced images taken over an acquisition time period of at least part of said human body into which said contrast agent passes, said procedure being a magnetic resonance imaging procedure, to detect temporal variations in said magnetic resonance signals or images;

detecting blood flow abnormality or flow variation in obstructed blood vessels in said body; and

identifying from said temporal variations in said images the blood flow abnormality.

39. (PREVIOUSLY PRESENTED) A method of detecting blood flow abnormality or variation in a blood vessel comprising:

administering a contrast enhancing amount of a paramagnetic metal containing

magnetic resonance contrast agent into a blood vessel of a body;

imaging at least a portion of the body through which the MR contrast agent passes, with a magnetic resonance imaging technique, thereby collecting temporally spaced sets of contour data and planar image data, each data set collected successively through an acquisition time;

forming a time sequence of image data including early image data within said acquisition time and later image data from within said acquisition time;

comparing contour data and planar image data from the temporally spaced sets of data by evaluating contour data and planar image data temporally acquired images by comparing ones of said early image data with ones of said later image data and their intensity to assess blood flow abnormality or variation.

40. (PREVIOUSLY PRESENTED) The method of claim 39 wherein said comparing step is carried out by a physician visually examining at least two sequenced images.

41. (PREVIOUSLY PRESENTED) The method of claim 39 wherein said comparing step is carried out by software quantitatively manipulating contour data and planar image data from at least two temporally spaced sets of data.

42. (NEW) A method of detecting and quantitatively evaluating an abnormality or variation in blood flow in a body, the method comprising the steps of:

(a) administering a magnetic resonance (MR) contrast agent into a blood vessel of a body, said MR contrast agent containing a contrast enhancing amount of a paramagnetic metal;

(b) scanning with an MR imaging scanner, according to a MR imaging procedure, at least a portion of the body through which said MR contrast agent passes to generate temporally spaced MR images thereof from MR signals induced therein;

(c) detecting temporal variations in said MR images by comparing at least one of said MR images acquired earlier in said scanning step with at least one of said MR images acquired later in said scanning step;

(d) identifying a region of abnormality or variation in blood flow using said temporal variations detected in said detecting step; and

(e) providing a quantitative indication of the abnormality or variation in blood flow in the region of the body identified in said identifying step.

43. (NEW) The method of claim 42 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent.

44. (NEW) The method of claim 42 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.

45. (NEW) The method of claim 42 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.

46. (New) The method of claim 44 wherein the paramagnetic metal is present as a chelate.

47. (New) The method of claim 46 wherein the Gd is present as a chelate.

48. (New) The method of claim 47 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.

49. (New) The method of claim 42 wherein the MR imaging procedure is selected from the group consisting of: T2\* weighted, T2 weighted and T1 weighted imaging sequences.

50. (New) The method of claim 49 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 8 minutes.

51. (New) The method of claim 49 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 5 minutes.

52. (New) The method of claim 42 wherein the desired MR imaging procedure is selected from the group consisting of spin echo imaging, gradient echo imaging and echo planar imaging.

53. (New) The method of claim 42 wherein the desired MR imaging procedure generates successive images in less than 0.5 seconds.

54. (New) The method of claim 42 wherein the desired MR imaging procedure generates successive images in less than 100 milliseconds.

55. (New) The method of claim 42 wherein said identifying step involves using results of the comparison of said detecting step to determine a ratio of signal intensity for each pixel/voxel in said MR images so compared and thereby identify the region of abnormality or variation in blood flow.

56. (New) The method of claim 42 wherein said identifying step involves a physician visually examining at least two of said MR images compared in said detecting step to identify the region of abnormality or variation in blood flow.

57. (New) The method of claim 42 wherein said step of providing a quantitative indication includes using results of the comparison of said detecting step to ascertain signal intensity versus time data and calculate therefrom at least one of (i) a corresponding numerical indication of the abnormality or variation in blood flow, (ii) a corresponding relative indication of the abnormality or variation in blood flow, and (iii) a corresponding percentage indication of the abnormality or variation in blood flow.

58. (New) The method of claim 57 wherein said signal intensity versus time data includes at least one of: (1) rate of change of signal intensity in said temporally spaced

MR images so compared, (2) degree of change in signal intensity in said temporally spaced MR images so compared, and (3) duration of change in signal intensity in said temporally spaced MR images so compared.

59. (New) The method of claim 42 further comprising the steps of:

(a) generating, in the absence of said MR contrast agent, at least one native MR image of the at least a portion of the body; and

(b) comparing the at least one native MR image with the at least one of said MR images acquired in the presence of said MR contrast agent;

so that said temporal variations detected in said detecting step include those detectable between the at least one native MR image and the at least one of said MR images acquired in the presence of said MR contrast agent.

60. (New) A method of detecting and quantitatively evaluating an abnormality or variation in blood flow in a body, the method comprising the steps of:

(a) administering a magnetic resonance (MR) contrast agent into a blood vessel of a body, said MR contrast agent containing a contrast enhancing amount of a paramagnetic metal;

(b) scanning with an MR imaging scanner, according to a desired MR imaging procedure, at least a portion of the body through which said MR contrast agent passes and thereby collecting sets of MR signal data corresponding to the at least a portion of the body, each of said sets of MR signal data being successively acquired over an acquisition time;

(c) detecting temporal variations in said MR signal data by comparing at least one earlier acquired set of said sets of MR signal data with at least one later acquired set of said sets of MR signal data;

(d) an identifying step comprising identifying a region of abnormality or variation in blood flow using said temporal variations detected in said detecting step; and

(e) providing a quantitative indication of the abnormality or variation in blood flow in the region of the body identified in said identifying step.

61. (New) The method of claim 60 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent.
62. (New) The method of claim 60 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.
63. (New) The method of claim 60 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.
64. (New) The method of claim 62 wherein the paramagnetic metal is present as a chelate.
65. (New) The method of claim 63 wherein the Gd is present as a chelate.
66. (New) The method of claim 65 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.
67. (New) The method of claim 60 wherein the desired MR imaging procedure is selected from the group consisting of: T2\* weighted, T2 weighted and T1 weighted imaging sequences.
68. (New) The method of claim 67 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 8 minutes.
69. (New) The method of claim 67 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 5 minutes.

70. (New) The method of claim 60 wherein the desired MR imaging procedure is selected from the group consisting of spin echo imaging, gradient echo imaging and echo planar imaging.

71. (New) The method of claim 60 wherein said sets of MR signal data includes at least one of 2-D planar image data and 3-D contour image data corresponding to the at least a portion of the body.

72. (New) The method of claim 71 wherein said identifying step involves:

(a) manipulating at least one of (I) said sets of 2-D planar image data and (II) said sets of 3-D contour image data to form a sequence of images of the at least a portion of the body; and

(b) comparing at least one earlier image in said sequence of images with at least one later image in said sequence of images so as to ascertain the abnormality or variation in blood flow.

73. (New) The method of claim 72 wherein said comparing step is carried out by a physician visually examining at least two images of said sequence of images.

74. (New) The method of claim 60 wherein said identifying step involves:

(a) manipulating said sets of MR signal data to form a sequence of images of the at least a portion of the body; and

(b) comparing at least one earlier image in said sequence of images with at least one later image in said sequence of images so as to ascertain the abnormality or variation in blood flow.

75. (New) The method of claim 74 wherein said comparing step is carried out by a physician visually examining at least two images of said sequence of images.

76. (New) The method of claim 71 wherein said identifying step is carried out by computer software quantitatively manipulating at least one of:



- (a) 2-D planar image data from at least two of said sets of 2-D planar image data; and
- (b) 3-D contour image data from at least two of said sets of 3-D contour image data.

77. (New) The method of claim 60 wherein said step of providing a quantitative indication includes using results of the comparison of said detecting step to ascertain signal intensity versus time data and calculate therefrom at least one of (i) a corresponding numerical indication of the abnormality or variation in blood flow, (ii) a corresponding relative indication of the abnormality or variation in blood flow, and (iii) a corresponding percentage indication of the abnormality or variation in blood flow.

78. (New) The method of claim 77 wherein said signal intensity versus time data includes at least one of: (1) rate of change of signal intensity in said sets of MR signal data so compared, (2) degree of change in signal intensity in said sets of MR signal data so compared, and (3) duration of change in signal intensity in said sets of MR signal data so compared.

79. (New) The method of claim 60 wherein each of said sets of MR signal data is acquired over said acquisition time of greater than 60 milliseconds.

80. (New) The method of claim 60 wherein each of said sets of MR signal data is acquired over said acquisition time of less than 5 seconds.

81. (New) The method of claim 80 wherein said MR contrast agent is administered at a dose in the range of 0.02 to 3 mmol per kilogram of bodyweight.

82. (New) The method of claim 60 wherein said MR contrast agent is administered at a dose in the range of 0.02 to 3 mmol per kilogram of bodyweight.

83. (New) The method of claim 60 wherein said MR contrast agent is administered at a dose in the range of 0.05 to 1.5 mmol per kilogram of bodyweight.

84. (New) The method of claim 60 wherein said sets of MR signal data each comprises a series of high speed echo planar images.

85. (New) The method of claim 60 wherein each of said sets of MR signal data provides the data necessary to form multiple images.

86. (New) A method of detecting an abnormality or variation in blood flow in a blood vessel of a body, the method comprising the steps of:

(a) administering a magnetic resonance magnetic resonance contrast agent into a vascular system of the body, said MR contrast agent containing a contrast enhancing amount of a paramagnetic metal;

(b) scanning with an MR imaging scanner, according to a desired MR imaging procedure, a region of the body containing the blood vessel through which said MR contrast agent passes thereby successively collecting MR signal data corresponding to the region of the body; and

(c) an analyzing step comprising analyzing said MR signal data by comparing at least one earlier acquired set of said MR signal data with at least one later acquired set of said MR signal data so as to ascertain the abnormality or variation in blood flow in the blood vessel.

87. (New) The method of claim 86 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent.

88. (New) The method of claim 86 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.

89. (New) The method of claim 86 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.

90. (New) The method of claim 89 wherein the paramagnetic metal is present as a chelate.

91. (New) The method of claim 90 wherein the Gd is present as a chelate.

92. (New) The method of claim 91 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.

93. (New) The method of claim 86 wherein the desired MR imaging procedure is selected from the group consisting of: T2\* weighted, T2 weighted and T1 weighted imaging sequences.

94. (New) The method of claim 93 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 8 minutes.

95. (New) The method of claim 93 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 5 minutes.

96. (New) The method of claim 86 wherein the desired MR imaging procedure is selected from the group consisting of spin echo imaging, gradient echo imaging and echo planar imaging.

97. (New) The method of claim 86 wherein said MR signal data includes at least one of 2-D planar image data and 3-D contour image data corresponding to the region of the body.

98. (New) The method of claim 97 wherein said analyzing step involves:

- (a) manipulating at least one of said 2-D planar image data and said 3-D contour image data to form a sequence of images of the region of the body; and
- (b) comparing at least one earlier image in said sequence of images with at least one later image in said sequence of images so as to ascertain the abnormality or variation in blood flow in the blood vessel.

99. (New) The method of claim 98 wherein said comparing step is carried out by a physician visually examining at least two images of said sequence of images.

100. (New) The method of claim 98 wherein said analyzing step further includes using results of said comparing step to ascertain signal intensity versus time data and calculate therefrom at least one of (i) a corresponding numerical indication of the abnormality or variation in blood flow, (ii) a corresponding relative indication of the abnormality or variation in blood flow, and (iii) a corresponding percentage indication of the abnormality or variation in blood flow.

101. (New) The method of claim 100 wherein said signal intensity versus time data includes at least one of: (1) rate of change of signal intensity in said images so compared, (2) degree of change in signal intensity in said images so compared, and (3) duration of change in signal intensity in said images so compared.

102. (New) The method of claim 86 wherein said analyzing step involves:

- (a) manipulating said MR signal data to form a sequence of images of the region of the body; and
- (b) comparing at least one earlier image in said sequence of images with at least one later image in said sequence of images so as to ascertain the abnormality or variation in blood flow in the blood vessel.

103. (New) The method of claim 102 wherein said comparing step is carried out by a physician visually examining at least two images of said sequence of images.

104. (New) The method of claim 103 wherein said analyzing step further includes using results of said comparing step to ascertain signal intensity versus time data and calculate therefrom at least one of (i) a corresponding numerical indication of the abnormality or variation in blood flow, (ii) a corresponding relative indication of the abnormality or variation in blood flow, and (iii) a corresponding percentage indication of the abnormality or variation in blood flow.

105. (New) The method of claim 104 wherein said signal intensity versus time data includes at least one of: (1) rate of change of signal intensity in said images so compared, (2) degree of change in signal intensity in said images so compared, and (3) duration of change in signal intensity in said images so compared.

106. (New) The method of claim 97 wherein said analyzing step is carried out by software quantitatively manipulating at least one of:

(a) said 2-D planar image data from at least one earlier acquired set of said 2-D planar image data with at least one later acquired set of said 2-D planar image data; and

(b) said 3-D contour image data from at least one earlier acquired set of said 3-D contour image data with at least one later acquired set of said 3-D contour image data.

107. (New) The method of claim 86 wherein each of said sets of MR signal data is acquired over an acquisition time of greater than 60 milliseconds.

108. (New) The method of claim 86 wherein each of said sets of MR signal data is acquired over an acquisition time of less than 5 seconds.

109. (New) The method of claim 108 wherein said MR contrast agent is administered at a dose in the range of 0.02 to 3 mmol per kilogram of bodyweight.

110. (New) The method of claim 86 wherein said MR contrast agent is administered at a dose in the range of 0.02 to 3 mmol per kilogram of bodyweight.

111. (New) The method of claim 86 wherein said MR contrast agent is administered at a dose in the range of 0.05 to 1.5 mmol per kilogram of bodyweight.

112. (New) The method of claim 86 wherein said sets of MR signal data each comprises a series of high speed echo planar images.

113. (New) The method of claim 86 wherein each of said sets of MR signal data provides the data necessary to form multiple images.

114. (New) A method of imaging a blood vessel in a body using magnetic resonance magnetic resonance imaging, the method comprising the steps of:

(a) acquiring images of a region of the body in which the blood vessel is located; and

(b) administering an MR contrast agent into a vascular system of the body at a dose and a time so that said MR contrast agent passing through the blood vessel is substantially at a maximum concentration during acquisition of said images thereof for at least part of said acquiring step.

115. (New) The method of claim 114 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent.

116. (New) The method of claim 114 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.

117. (New) The method of claim 114 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.

118. (New) The method of claim 116 wherein the paramagnetic metal is present as a chelate.
119. (New) The method of claim 117 wherein the Gd is present as a chelate.
120. (New) The method of claim 119 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.
121. (New) The method of claim 114 wherein said MR contrast agent is administered at a dose in the range of 0.02 to 3 mmol per kilogram of bodyweight.
122. (New) The method of claim 114 wherein said MR contrast agent is administered at a dose in the range of 0.05 to 1.5 mmol per kilogram of bodyweight.
123. (New) The method of claim 114 wherein said acquiring step employs a procedure selected from the group consisting of: T2\* weighted, T2 weighted and T1 weighted imaging sequences.
124. (New) The method of claim 123 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 8 minutes.
125. (New) The method of claim 123 wherein said T2\* weighted, T2 weighted and T1 weighted imaging sequences each have an image acquisition time of less than 5 minutes.
126. (New) The method of claim 124 wherein said acquiring step employs a procedure selected from the group consisting of spin echo imaging, gradient echo imaging and echo planar imaging.
127. (New) A method of imaging a blood vessel in a body using magnetic resonance magnetic resonance imaging, the method comprising the steps of:

(a) administering an MR contrast agent into a vascular system of the body, said MR contrast agent containing a contrast enhancing amount of a paramagnetic metal; and

(b) acquiring images of a region of the body in which the blood vessel is located before, during and after administration of said MR contrast agent;

with said images acquired before administration of said MR contrast agent capable of comparison with at least said images acquired while said MR contrast agent passing through the blood vessel is substantially at a maximum concentration.

128. (New) The method of claim 127 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent.

129. (New) The method of claim 127 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.

130. (New) The method of claim 127 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.

131. (New) The method of claim 129 wherein the paramagnetic metal is present as a chelate.

132. (New) The method of claim 130 wherein the Gd is present as a chelate.

133. (New) The method of claim 132 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.

134. (New) A method of imaging a blood vessel in a body using magnetic resonance magnetic resonance imaging, the method comprising the steps of:



- (a) acquiring images of a region of the body in which the blood vessel is located; and
- (b) administering an MR contrast agent into a vascular system of the body at a dose and a time selected so that said MR contrast agent passing through the blood vessel is present therein during acquisition of said images thereof for at least part of said acquiring step.

135. (New) The method of claim 134 wherein said MR contrast agent is provided in a form selected from the group consisting of particulate forms, hydrophilic forms, and blood-pooling forms of the contrast agent. (New) The method of claim H1 wherein the paramagnetic metal contained within said MR contrast agent is selected from the group consisting of Cr, V, Mn, Fe, Co, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Tb and Ln.

136. (New) The method of claim 134 wherein the paramagnetic metal contained within said MR contrast agent comprises Gd.

137. (New) The method of claim 136 wherein the paramagnetic metal is present as a chelate.

138. (New) The method of claim 137 wherein the Gd is present as a chelate.

139. (New) The method of claim 138 wherein the chelate of Gd comprises material selected from the group consisting of Gd-D03A, GdDTPA-BMA and GdDTPA-BMO.